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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/587,320	05/10/2007	Noriaki Kato	868_012	4731

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EXAMINER	
WESTERBERG, NISSA M	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
03/18/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/587,320	KATO ET AL.	
	Examiner	Art Unit	
	Nissa M. Westerberg	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *10 -14* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *10 - 14* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 July 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *7/26/06; 12/17/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Claim Rejections - 35 USC § 112 1st Paragraph

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claims 10 – 14 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for ameliorating diabetic maculopathy, does not reasonably provide enablement for a method for preventing diabetic maculopathy. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The disclosure and claims of the application have been compared per the factors indicated in the decision *In re Wands*, 8 USPQ2nd 1400 (Fed. Cir. 1988) as to undue experimentation

The factors include:

1. The nature of the invention;
2. The breadth of the claims;
3. The predictability or unpredictability of the art;
4. The amount of direction or guidance presented;
5. The presence or absence of working examples

6. The quantity of experimentation necessary;

7. The state of the prior art; and

8. The relative skill of those skilled in the art.

Each factor is address below on the basis of comparison of the disclosure, the claims and the state of the art in the assessment of undue experimentation.

1. The nature of the invention and breadth of the claims: A method of preventing or ameliorating diabetic maculopathy in a mammal comprising administering an effective amount of a compound represented by the formula in claim 10. That structure contains three variable substituents.

2. The amount of direction or guidance presented, the presence or absence of working examples: Examples are provided in which SNK-860, the compound of claim 12, is administered to diabetic rats and monkeys, and the anatomy of the eye at various times was determined.

3. The predictability or unpredictability of the art, the quantity of experimentation necessary, the state of the prior art, and the relative skill of those skilled in the art: The relative skill of those skilled in the art is high. This compound has been used in the art to treat diabetic patients. “Prevent” is defined as to keep from happening, make impossible or stop from being in a certain state (p 3, dictionary.com definition, accessed 11/28/07).

Therefore, prevention of diabetic maculopathy means that the subject would never develop this condition. It has not been shown that administration of this compound will mean that the subjects will never develop this condition. Therefore, Applicants have are enabled for using compounds of the specified formula for the amelioration of diabetic maculopathy but are not enabled for the prevention of diabetic maculopathy. Due to the various factors in developing diabetes, e.g., heredity/predisposition, diet, age, etc., as well as, various unknown factors, there is no known drug that can "prevent" diabetes. Thus, the unpredictability is very high in this area and some guidance must be presented. However, the instant specification, or what is known in the art shows no guidance on actually preventing diabetes, as claimed. Thus, it would require undue experimentation to determine how, and in which circumstances, diabetes could, in fact, be prevented.

Claim Rejections - 35 USC § 112 2nd Paragraph

3. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 10, 11, 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The formula of claim 10 contains an NR^1R^2 substituent and in the definition of R^1 and R^2, the phrase “together with a nitrogen atom bound thereto” appears. It is unclear whether the N, to which R^1 and R^2

are attached is in the 5- or 6-membered heterocyclic ring, along with an additional but optional nitrogen or an oxygen atom or if the nitrogen atom shown in the formula serves as the attachment point for the 5- or 6-membered heterocyclic ring that can contain one nitrogen or one oxygen atom.

5. Claims 13 and 14 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. These claims recite a method "for use in" language that attempts to further define particular aspect of diabetic maculopathy being treated. It is unclear whether applicant intended to another step to be present in the method or was simply further refining the patient population to be treated.

Claim Rejections - 35 USC § 103

6. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

7. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

8. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

9. Claims 10 – 14 are rejected under 35 U.S.C. 103(a) as being unpatentable over Masahiko Akita et al. (Acta Med Okayama 1993, cited on PTO-1449) in view of Lopes de Faria et al. (Acta Opthalmol Scand 1999).

Masahiko Akita et al. discloses the use of SNK-980, the compound of claim 12, as an aldose reductase inhibitor for the treatment of histopathological changes in retinal tissues (p 299, col 1 – col 2). In a diabetic rat model, SNK-860 was administered orally (p 300, col 1, paragraph 2). Diabetic rats that were not administered SNK-860 developed pathological folding of the retina with retinal edema or cell dissociation that was not seen in non-diabetic rats or diabetic rats given SNK-860 (p 300, col 2,

paragraph 5). Leakage of albumin from the blood vessels in the area under these folds of diabetic rats not receiving SNK-860 was also observed (p 302, col 2, paragraph 2).

Masahiko Akita et al. does not disclose the use of SNK-860 for the treatment of diabetic maculopathy or diabetic edema.

Lopes de Faria et al. discloses that diabetic retinopathy (DR) is the most important ocular complication in patients with diabetes (p 170, col 1, paragraph 1). Complications that can develop as a result of DR include two types of DR (proliferative and nonproliferative) and macular edema. The latter represents the major cause of vision loss in patients with DR (p 170, col 2, paragraph 1) and can results from ischemia, retinal edema or both (p 170, col 3, paragraph 3). Patients with either type of DR were found to have an increased risk of developing macular edema (p 174, col 1, paragraph 2) and severe DR was associated with increased risk of developing diffuse macular edema (p 174, col 1, paragraph 4).

It would have been obvious to one of ordinary skill in the art at the time of the instant invention to use SNK-860 to treat diabetic maculopathy because Masahiko Akita et al. discloses that this compound is useful for treating DR and symptoms asscoaited with other eye conditions that commonly occur in diabetic patients. Lopes de Faria et al. teaches that administration of this compound to diabetic mice decreases changes in the retina such as folding, retinal edema and leakage of blood components like albumin from the blood vessels of the retina. Abnormal fluid balance and protein deposits are characteristics of macular edema. Rats administered SNK-860 did not develop such changes over the course of the experiment. Since SNK-860 has been shown to be

effective in treating a condition that is a significant risk factor for macular edema and diabetic maculopathy, as well as inhibiting retinal edema, one of ordinary skill in the art would have a reasonable expectation of success in using SNK-860 to ameliorate diabetic maculopathy as it is useful in treating other eye conditions commonly found in diabetics. This treatment would also prevent further deterioration of visual acuity by treating the underlying problems that lead to decreased visual acuity.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Nissa M. Westerberg whose telephone number is (571)270-3532. The examiner can normally be reached on M - F, 8 a.m. - 4 p.m. ET. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Michael G. Hartley/
Supervisory Patent Examiner, Art Unit 1618

NMW